

**WHAT IS CLAIMED IS:**

1. A method of detecting a polynucleotide-polypeptide interaction domain in a genome of an organism, comprising:
  - a) immunoprecipitating a polynucleotide associated with a polypeptide to obtain an enriched polynucleotide preparation;
  - b) dissociating the polynucleotide and polypeptide in the enriched preparation;
  - c) contacting the polynucleotide with a primer pair under conditions whereby the primer pair hybridizes to the polynucleotide to form a first hybridization complex, each primer comprising at least two portions, a first portion comprising a target-specific oligonucleotide that is capable of hybridizing to a target polynucleotide in the enriched preparation, and a second portion comprising a universal primer landing site, the two primers being specific for an upstream and downstream segment of the target polynucleotide, wherein the universal landing sites are not the same;
  - d) contacting the first hybridization complex with a ligase under conditions whereby primer pairs hybridized to the polynucleotide are ligated to form a ligated probe;
  - e) amplifying the ligated probe with universal primers to generate an amplified-labeled product;
  - f) contacting the amplified-labeled product with an array of oligonucleotides under conditions whereby the ligated probe hybridizes to a complementary oligonucleotide in the array to form assay complexes; and
  - g) detecting the assay complexes, wherein the presence of complexes is indicative of DNA that binds the immunoprecipitated polypeptide.

2. The method of claim 1, wherein the polynucleotide associated with the polypeptide are crosslinked polynucleotide-polypeptide complexes.
3. The method of claim 2, wherein the crosslinking of the polynucleotide and polypeptide is performed by UV light, formaldehyde, psorelan, or any combination thereof.
4. The method of claim 1, wherein the universal landing sites are selected from a T3 and T7 priming site.
5. The method of claim 1, wherein the universal primers comprise a detectable label.
6. The method of claim 5, wherein the detectable label is selected from the group consisting of an isotopic label; a magnetic, electrical, or thermal label; an enzymatic label; and a fluorescent or luminescent label.
7. The method of claim 6, wherein the isotopic label comprises a radioactive or heavy isotopes.
8. The method of claim 6, wherein the fluorescent or luminescent label is selected from the group consisting of fluorescent lanthanide complexes, Europium, Terbium, fluorescein, rhodamine, tetramethylrhodamine, eosin, erythrosin, coumarin, methyl-coumarins, quantum dots, pyrene, Malacite green, stilbene, Lucifer Yellow, Cascade Blue™, Texas Red, Cy dyes, alexa dyes, phycoerythrin, and bodipy.

9. A method of detecting a polynucleotide-polypeptide interaction domain in a genome of an organism, comprising:
- a) crosslinking a DNA binding protein to genomic DNA of the organism, thereby producing DNA-protein complexes;
  - b) fragmenting the DNA-protein complexes to produce a mixture comprising DNA fragment-protein complexes;
  - c) removing a DNA fragment-protein complex from the mixture produced in b);
  - d) separating the DNA fragment obtained in c) from the DNA binding protein;
  - e) contacting the DNA with a primer pair under conditions whereby the primer pair hybridizes to the DNA fragment to form a first hybridization complex, each primer comprising at least two portions, a first portion comprising a target-specific oligonucleotide that is capable of hybridizing to the DNA fragment, and a second portion comprising a universal primer landing site, the two primers designed to be specific for an upstream and downstream segment of the DNA fragment, wherein the universal landing sites are not the same;
  - f) contacting the first hybridization complex with a ligase under conditions whereby primer pairs hybridized to the DNA fragment are ligated to form a ligated probe;
  - g) contacting the ligated probe with universal primers;
  - h) amplifying the ligated probe of g) to obtain an amplified product;
  - i) combining the amplified product of h) with complementary polynucleotides from the organism under conditions in which hybridization between the amplified product and a region of the complementary polynucleotide occurs to form a second hybridization complex; and

- j) identifying the second hybridization complex of i), wherein the second hybridization complex comprises the region of the genome to which the DNA binding protein interacts.
10. The method of claim 9, wherein the organism is a eukaryotic cell.
11. The method of claim 9, wherein the organism is a prokaryotic cell.
12. The method of claim 9, wherein the DNA binding protein is a transcription factor.
13. The method of claim 9, wherein the DNA binding protein of the cell is crosslinked to the genomic DNA of the organism using formaldehyde, psorelan, and/or UV light.
14. The method of claim 9, wherein the DNA is fragmented using a restriction enzyme and/or sonication.
15. The method of claim 9, wherein the DNA fragment-protein complex is removed using an antibody which binds to the protein.
16. The method of claim 9, wherein the ligated probe of h) is amplified using ligation-mediated polymerase chain reaction.
17. The method of claim 9, wherein the second hybridization complex is formed on a DNA microarray.

18. The method of claim 9, wherein the universal primer landing sites are selected from a T3 and T7 priming site.
19. The method of claim 9, wherein the universal primers comprise a detectable label.
20. The method of claim 19, wherein the detectable label is selected from the group consisting of an isotopic label; a magnetic, electrical, or thermal label; an enzymatic label; and a fluorescent or luminescent label.
21. The method of claim 20, wherein the isotopic label comprises a radioactive or heavy isotopes.
22. The method of claim 20, wherein the fluorescent or luminescent label is selected from the group consisting of fluorescent lanthanide complexes, Europium, Terbium, fluorescein, rhodamine, tetramethylrhodamine, eosin, erythrosin, coumarin, methyl-coumarins, quantum dots, pyrene, Malacite green, stilbene, Lucifer Yellow, Cascade Blue™, Texas Red, Cy dyes, alexa dyes, phycoerythrin, and bodipy.
23. A method of identifying a region of a genome of a living cell to which a polypeptide of interest binds, comprising:
  - a) crosslinking DNA binding polypeptides in the living cell to genomic DNA of the living cell, thereby producing DNA binding polypeptides crosslinked to genomic DNA;
  - b) generating DNA fragments of the genomic DNA crosslinked to DNA binding polypeptides, thereby producing DNA fragments to which DNA binding polypeptides are bound;

- c) immunoprecipitating a DNA fragment using an antibody that specifically binds the polypeptide of interest;
- d) separating the DNA fragment obtained in c) from the polypeptide of interest;
- e) contacting the DNA fragment with a primer pair under conditions whereby the primer pair hybridizes to the DNA fragment to form a first hybridization complex, each primer comprising at least two portions, a first portion comprising a target-specific oligonucleotide that is capable of hybridizing to the DNA fragment, and a second portion comprising a universal primer landing site, the two primers are designed to be specific for an upstream and downstream segment of the DNA fragment, wherein the universal landing sites are not the same;
- f) contacting the first hybridization complex with a ligase under conditions whereby the primer pairs hybridized to the DNA fragment are ligated to form a ligated probe;
- g) amplifying the ligated probe of f) using universal primers labeled with a detectable label to obtain an amplified product;
- h) combining the amplified product of g) with complementary polynucleotides from the cell, under conditions in which hybridization between the amplified product and a region of the complementary polynucleotide occurs to form a second hybridization complex; and
- i) identifying the second hybridization complex of h) using methods specific for the label, wherein the second hybridization complex comprises the region of the genome in the cell to which the polypeptide of interest binds.

24. The method of claim 23, further comprising comparing the label intensity/amount measured in i) to the

amount/intensity of a control, wherein amount/intensity of the label in a region of the genome which is greater than the amount/intensity of label of the control in the region indicates the region of the genome in the cell to which the polypeptide of interest binds.

25. The method of claim 23, wherein the cell is a eukaryotic cell.

26. The method of claim 23, wherein the cell is a prokaryotic cell.

27. The method of claim 23, wherein the DNA binding polypeptide is a transcription factor.

28. The method of claim 23, wherein the DNA binding polypeptide is crosslinked to the genomic DNA of the cell using formaldehyde, psorelan, and/or UV light.

29. The method of claim 23, wherein the DNA is fragmented using a restriction enzyme and/or sonication.

30. The method of claim 23, wherein the ligated probe of f) is amplified using ligation-mediated polymerase chain reaction.

31. The method of claim 23, wherein the second hybridization complex is formed on a DNA microarray.

32. The method of claim 23, wherein the universal primer landing sites are selected from a T3 and T7 priming site.

33. The method of claim 23, wherein the universal primers comprise a detectable label.

34. The method of claim 33, wherein the detectable label is selected from the group consisting of an isotopic label; a magnetic, electrical, or thermal label; an enzymatic label; and a fluorescent or luminescent label.

35. The method of claim 34, wherein the isotopic label comprises a radioactive or heavy isotopes.

36. The method of claim 33, wherein the fluorescent or luminescent label is selected from the group consisting of fluorescent lanthanide complexes, Europium, Terbium, fluorescein, rhodamine, tetramethylrhodamine, eosin, erythrosin, coumarin, methyl-coumarins, quantum dots, pyrene, Malacite green, stilbene, Lucifer Yellow, Cascade Blue™, Texas Red, Cy dyes, alexa dyes, phycoerythrin, and bodipy.

37. A kit comprising:

means for immunoprecipitating a polynucleotide associated with a polypeptide to obtain an enriched polynucleotide preparation;

a primer pair, each primer comprising at least two portions, a first portion comprising a target-specific oligonucleotide that is capable of hybridizing to a target polynucleotide in the enriched preparation, and a second portion comprising a universal primer landing site, the two primers being specific for an upstream and downstream segment of the target polynucleotide, wherein the universal landing sites are not the same;

a ligase;  
universal primers; and  
an array of oligonucleotides.